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EXAMINER	
SALVOZA, M FRANCO G	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,226	BUSCHER ET AL.	
	Examiner	Art Unit	
	M. Franco Salvoza	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08/05/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-117* is/are pending in the application.

4a) Of the above claim(s) *58-117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 58-117 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 5. 2005.

Applicant argued that Group II be reclassified with Group I for reciting a chemistry method that includes determining antiviral activity against two or more viruses, and Groups III, IV and V be reclassified for reciting broader than implementation by a data processing system, a requirement for classification in class 705.

Applicant's arguments are considered and found persuasive for Group II, but unpersuasive to Groups III, IV and V. Group II is drawn to a method of rating compounds for antiviral efficacy, which has been properly amended to become part of claim 43 and Group I, drawn to a method for identifying antiviral compounds and determining antiviral activity. However, Groups III, IV and V are drawn to marketing and business methods that, as applicant cites, can be supported or implemented by a data processing system.

The restriction is maintained and made FINAL for reasons of record, and upon filing of divisional or continuation applications the claims may be reclassified depending on future subject matter.

Claims 43, 49 and 50 have been amended. Claims 1-57 are pending and under consideration.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on p. 20. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The abstract of the disclosure is objected to because the first phrase does not constitute a sentence. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites a method for identifying a broad-spectrum antiviral lead compound comprising determining antiviral activity of a plurality of compounds against two or more viruses and identifying a broad spectrum antiviral lead compound from the plurality of compounds, said lead compound having activity against at least two of the two or more viruses. It is presumed from the recitation on p. 8 of the specification that the recitation to "two or more viruses" means two or more distinct species, geni, subgeni or families of viruses rather than two or more virus units. However, based on the language of the claim it can be construed in both ways and appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 32-34, 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In this case, claims 1-3, 32-34, 43-45 recite the subgenomic viral replication system that is selected from a group consisting of a defective genome, a minigenome, an amplicon and a replicon. If the replication system contains a defective genome, the invention will not be able to identify a lead compound with antiviral activity. If the virus or replication system to be identified is defective, the invention cannot identify it.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-10, 12, 17, 18, 21- 23, 26, 30-39, 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonyhadi et al. (U.S. Patent. #5,645,982), which was issued on July 8, 1997, more than one year before applicant's filing date of January 28, 2004.

Claims 1-4 recite a method for identifying a broad-spectrum antiviral lead compound comprising determining antiviral activity of a plurality of compounds against two or more

viruses and identifying a broad-spectrum antiviral lead compound from the plurality of compounds said lead compound having activity against at least two of the two or more viruses; wherein determining antiviral activity of each of the plurality if compounds against at least one subgenomic viral replication system representative of at least one of the two or more viruses; wherein the subgenomic viral replication system is selected from a group consisting of a defective genome, a minigenome, an amplicon and a replicon; wherein identifying is a function of the determined antiviral activity and a number of the two or more viruses for which the lead compound has antiviral activity.

Bonyhadi et al. teaches a method for screening potential therapeutically effective antiviral agents including determining antiviral activity of a plurality of compounds (here, AZT and ddI; column 12, line 47) against two or more viruses (here, two strains of HIV – EW and NL4-3; column 15, line 1) that had activity against at least two of the two or more viruses (Tables 6a, 6b, 7a, 7b columns 15-18). The antiviral activity tested was for virus replication of the HIV minigenome – "the data indicates that both ddI and AZT inhibit viral replication in thymic lobule culture system, even when administered at sub-micromolar levels" (column 12, line 53).

Claims 7, 8, 32-35 recite the method wherein the identified broad-spectrum antiviral lead compound has antiviral activity greater than a predetermined threshold antiviral activity against each of at least two of the two or more viruses; wherein the two or more viruses comprise two or more viruses from one viral family and the identified broad-spectrum antiviral lead compound has activity greater than a predetermined threshold antiviral activity against at least two viruses of the two or more viruses from the one viral family.

Claims 32-35 recite a method for identifying a class of broad-spectrum antiviral compounds, the method comprising determining antiviral activity of compounds from two or more classes of compounds against two or more viruses, each of said classes of compounds having one or more member compounds and identifying a class of broad spectrum antiviral compounds, said class of broadspectrum antiviral compounds having a member compound with antiviral activity greater than a predetermined threshold antiviral activity against a plurality of the two or more viruses; wherein determining comprises determining antiviral activity of each compound against at least one subgenomic viral replication system representative of at least one of the two or more viruses; wherein the subgenomic viral replication system is selected from a group consisting of a defective genome, a minigenome, an amplicon and a replicon; the method of claim 32 wherein the two or more viruses comprise two or more viruses from one viral family and the identified class of broad-spectrum antiviral compounds has activity greater than the predetermined threshold antiviral activity against at least two viruses of the two or more viruses from the one viral family.

Bonyhadi et al. teaches the screening of broad classes of anti-viral agents (column 5, line 4) in human thymic lobules as well as the use of control samples for predetermined threshold antiviral activity as a basis for comparison, wherein "the agent is a potential anti-viral agent if it suppresses viral pathology relative to lobules incubated in a control sample" (column 4, line 11).

Claims 9, 10, 12, 17, 18, 26, 36, 38 recite the methods wherein: the method of claim 1 wherein the two or more viruses are RNA viruses; wherein the two or more viruses are positive strand RNA viruses; wherein the two or more viruses are selected from a group including rubella; wherein the two or more viruses are RNA retroviruses; wherein the two or

more viruses are selected from a group consisting of HIV-1, HIV-2, HTLV-1, and HTLV-2; wherein the two or more viruses are selected from a group consisting of RNA viruses and DNA viruses. Claim 36 recites the method of claim 32 wherein the two or more viruses are RNA viruses; wherein the two or more viruses are selected from a group consisting of positive-strand RNA viruses, negative-strand RNA viruses, RNA reverse transcribing viruses, double strand RNA viruses and DNA viruses.

Bonyhadi et al. teaches the screening method for HIV, a positive strand RNA retrovirus (column 4, line 6), and rubella (column 4, line 60).

Claims 21, 22, 23, 30, 31, 37, 39, 42 recite the methods wherein: the two or more viruses are DNA viruses; or from one or more families selected from a group consisting of herpesviridae (claim 22, 30); from a group consisting of herpes simplex virus (claim 23, 31); the method of claim 32 wherein the two or more viruses are DNA viruses; wherein the two or more viruses are from one or more virus families selected from a group consisting of herpesviridae, etc.; the method of claim 32 wherein the two or more viruses are selected from a group including herpes simplex virus.

Bonyhadi et al. teaches the screening method for human cytomegalovirus and herpes simplex virus (column 4, line 57-60).

Claims 1, 2, 3, 4, 7, 8, 11, 13-16, 19, 20, 24, 25, 27, 28, 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Miles et al. (U.S. Patent. #5,738,985), which was issued on April 14, 1998, more than one year before applicant's filing date of January 28, 2004.

Claims 1, 2, 3, 4 recite a method identifying a broad-spectrum antiviral lead compound comprising determining antiviral activity of a plurality of compounds against two or more

viruses and identifying a broad-spectrum antiviral lead compound from the plurality of compounds said lead compound having activity against at least two of the two or more viruses; wherein determining antiviral activity of each of the plurality if compounds against at least one subgenomic viral replication system representative of at least one of the two or more viruses; wherein the subgenomic viral replication system is selected from a group consisting of a defective genome, a minigenome, an amplicon and a replicon; wherein identifying is a function of the determined antiviral activity and a number of the two or more viruses for which the lead compound has antiviral activity.

Miles et al. teaches methods for screening for potential antiviral agents in which "a large number of potentially useful agents are processed in the method of this invention. It is generally a process distinct from a single experiment in which a single agent is studied in detail to determine its method of action" (column 3, line 47). Miles et al. teaches a broad class of potential antiviral agents that interact with a viral inhibitor or agent that allows preferential translation of viral RNA are screened in order to determine their effects on viral replication. For example, Miles et al. teaches transfection-infection assays to screen for agents that block 5' UTR influenza virus activity in host cells (column 57, line 52; column 59, line 3), and teaches animal models infected with strains of rhinoviruses (column 80, line 65).

Claims 7, 8 recite the method of claim 1 wherein the identified broad-spectrum antiviral lead compound has antiviral activity greater than a predetermined threshold antiviral activity against each of at least two of the two or more viruses; wherein the two or more viruses comprise two or more viruses from one viral family and the identified broad-spectrum antiviral lead

compound has activity greater than a predetermined threshold antiviral activity against at least two viruses of the two or more viruses from the one viral family.

Miles et al. teaches the use of selective protocols compared with control data in order to determine the extent of antiviral activity (Example 3, column 27) in screening of p68 kinase.

Claims 13, 14, 15, 16 recite the method of claim 1 wherein the two or more viruses are negative strand RNA viruses; wherein the two or more viruses are from one or more virus families from a group consisting of Paramyxoviridae, Rhabdoviridae, Filoviridae, Orthomyxoviridae, Bunyaviridae, Bornaviridae, and Arenaviridae; wherein the two or more negative-strand RNA viruses; wherein the two or more viruses are selected from a group consisting of RSV, Ebola virus, rabies virus, Lassa fever, Argentine hemorrhagic fever virus, La Crosse virus, Rift Valley fever, etc.

Miles et al teaches the method of screening for protein inhibitors used by influenza viruses, which are included in the family of Orthomyxoviridae (column 39, line 56).

Claims 19, 20 recite the method of claim 1 wherein the two or more viruses are double strand RNA viruses; wherein the two or more viruses include a virus from a Reoviridae virus family.

Miles et al. teaches use of the screening methods for viral RNAs interfering with protein kinases such as p68 kinase that as used by reovirus (column 12, line 34).

Claims 24, 25 recite the method of claim 1 wherein the two or more viruses are DNA reverse transcribing viruses; wherein the two or more viruses includes a virus from Hepadnaviridae family.

Miles et al. teaches the use of the screening methods for inhibitors of viral nucleic acids used to translate viral proteins for Hepatitis B, included in the family of Hepadnaviridae (column 38, line 66).

Claims 11, 27, 28, recite the method of claim 1 wherein the two or more viruses are from one or more virus families selected from a group consisting of Picornaviridae, Caliciviridae, Astroviridae, Coronaviridae, Togaviridae and Flaviviridae; wherein the two or more viruses are selected from a group; wherein the two or more viruses are selected from a group consisting of respiratory syncytial virus and hepatitis C virus.

Claim 40 recites the method of claim 32 wherein the two or more viruses are selected from a group consisting of respiratory syncytial virus and hepatitis C virus.

Miles et al. teaches use of the screening methods for viral nucleic acids used to translate viral proteins for Hepatitis C, a member of the genus of Flaviviridae (column 39, line 39).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 43-45, 47, 48, 49, 50-54, 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonyhadi et al.

Claims 1, 6, 43-45, 47, 48, 49, 50-54, 57 recite the methods of identifying a broad spectrum antiviral lead compound comprising determining antiviral activity for each of a

plurality of compounds against two or more viruses; rating each compound for broad spectrum activity as a function of the determined antiviral activity and a number of the two or more viruses for which each compound has antiviral activity and identifying a broad-spectrum antiviral lead compound from the plurality of compounds as a function of the rating of each compound, said lead compound having activity against at least two of the two or more viruses. Claim 49 recites the method of claim 43 further comprising developing a broad-spectrum antiviral drug from the identified broad-spectrum antiviral lead compound.

Claim 51 recites the method of claim 43 wherein the two or more viruses are RNA viruses; claim 52 recites the method of claim 43 wherein the two or more viruses are DNA viruses; claim 53 recites the method of claim 43 wherein the two or more viruses are selected from a group consisting of positive strand RNA viruses, negative strand RNA viruses, RNA reverse transcribing viruses, double strand RNA viruses, and DNA viruses. Claim 54 recites the method of claim 43 wherein the two or more viruses are from one or more virus families selected from a group consisting of herpesviridae, etc; claim 57 recites the method of claim 43 wherein the two or more viruses are from one or more virus families selected from a group consisting of herpes simplex, etc.

See the teachings of Bonyhadi et al. In addition, Bonyhadi et al. teaches developing the antiviral agent in response to claim 49: "use of drugs or other agents with known mechanistic targets can delineate new elements of viral pathology, thereby providing new targets for intervention through cellular therapy, gene therapy, drug therapy, or rational drug design" (column 6, lines 37).

However, Bonyhadi et al. does not teach rating each of the plurality of compounds for antiviral activity.

One of ordinary skill in the art at the time the invention was made would have been motivated to use a rating and prioritizing system while collecting data along with the method for identifying and determining antiviral activity of Bonyhadi et al. for the cited species in order to evaluate the effectiveness against other compounds used. Applicant in Response to the Requirement for Restriction/Election states: "While the claim 43 also recites rating each compound for broad-spectrum activity as a function of the determined antiviral activity and a number of viruses for which each compound has antiviral activity, this again is a typical process performed by a chemist."

One of ordinary skill in the art at time to the invention was made would have had a reasonable expectation of success for using a method of rating to analyze data and prioritize results.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 1, 29, 32, 41, 43, 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miles et al.

Claims 1, 29, 32, 41 recite the methods of identifying and determining antiviral activity wherein the viruses are selected from a group consisting of viral species of West Nile virus, yellow fever virus, Sindbis virus, Venezuela encephalitis virus and Ebola virus as targets for screening.

See the teachings of Miles et al. One of ordinary skill in the art at the time the invention was made would have been motivated to use the method for identifying and determining antiviral activity of Miles et al. for the cited species of claims 29, 41, 55 and 56 in order to screen for pathogenic activity in other viral species of common to the flavivirus family of the recited Hepatitis C such as Yellow Fever virus and West Nile virus.

Claim 55 recites the method of claim 43 wherein the two or more viruses are selected from a group consisting of respiratory syncytial virus and hepatitis C virus. Claim 56 recites the method of claim 43 wherein the viruses are selected from a group consisting of viral species of West Nile virus, yellow fever virus, Sindbis virus, Venezuela encephalitis virus and Ebola virus as targets for screening.

As to claim 55 and 56, one of ordinary skill in the art would have also been motivated to use a rating and prioritizing system along with the method for identifying and determining antiviral activity of Miles et al. for the cited species in order to evaluate the effectiveness against other compounds used.

One of ordinary skill in the art at time at the invention was made would have had a reasonable expectation of success for using the methods for identifying and determining antiviral activity of Miles et al. with the species cited because of the common viral family and species characteristics. One of ordinary skill in the art at time at the invention was made would have had a reasonable expectation of success for using a method of rating to analyze data and prioritize results.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the

contrary.

Claims 1, 5, 43 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonyhadi et al. in view of Jiang et al. (U.S. Patent # 6,596,497).

Claims 1, 5, 43 and 46 recite the methods wherein the determining of antiviral activity for each of the plurality of compounds comprises determining activity using one or more of the group consisting of an EC50, a CC50 and a Selectivity Index.

See the teachings of Bonyhadi et al. Bonyhadi et al. does not teach the use of an effective concentration measure, inhibitory concentration measure or selectivity index is a way to rate and measure antiviral activity for a plurality of compounds. Jiang et al. uses the rating and measuring method of a Selectivity Index as a way to measure inhibitory activity by dividing cytotoxicity concentrations by inhibitory concentration (column 29, line 61).

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the methods of identifying and determining antiviral activity of Bonyhadi et al. and the selectivity index rating method of Jiang et al. because Jiang et al. teaches measuring methods to effectively measure and compare cytotoxic activity.

One of ordinary skill in the art at time at the invention was made would have had a reasonable expectation of success for using the methods of identifying and determining antiviral activity of Bonyhadi et al. with the selectivity index rating method of Jiang et al. because Bonyhadi et. al. and Jiang et al. both teach using standard methods for measuring and evaluating antiviral activity after screening protocols.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the

contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. Franco Salvoza
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10/31/05

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